The Diagnostic Problem in Asthma

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SUMMARY

Differences in the types of asthma are due to differences in the cause of the condition. As determination of the type is important with regard to treatment and prognosis, "etiologic diagnosis" is a principal problem.

Observers in various parts of the country may disagree sharply as to the relative incidence of one type and another, a disagreement which may be based on differences in the environments in which they make their observations.

Reaching agreement on the interpretation of symptoms would be of great value. It must come from further careful, unbiased observation.

WITH the accumulation of knowledge regarding the conditions which cause dyspnea, the differential diagnosis of bronchial asthma has become comparatively easy. There is seldom any reason for confusion if one takes advantage of the means available to determine definitely what the condition may be. It is possible, of course, for asthma and some other condition causing dyspnea to coexist; and this may make it somewhat difficult to know whether the condition is true asthma, and, if so, just how much of the dyspnea may be due to asthma and how much to the other condition. Even this usually can be determined by observation over a short period.

To aid in the clarification of thinking on the subject, it is desirable to abandon the use of such terms as cardiac asthma and renal asthma. With the recognition of many causes of dyspnea, this term should no longer be used as synonymous with asthma, and in the light of present knowledge of the physiology and pathology of cardiac and renal function, other terms should be used to describe the dyspnea which may accompany cardiac or renal disease. Failure to make this distinction, both in diagnosis and in terminology, is the reason for inability to evaluate histories and statistics of former years and thus to know just how much asthma has existed and what the morbidity and mortality rates may have been.

Errors in differentiation may still occur, but they are usually due to failure to use the means available.

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The problem is not in the diagnosis of asthma but in the determination of the type of asthma. Asthma varies a great deal in etiology, symptomatology and prognosis, and the correct determination of the type of asthma is of importance in determining treatment and estimating the prognosis. These differences in type of asthma are due to the differences in the cause of the condition, so that the problem is one of "etiologic diagnosis." This does not mean simply determining whether the patient is sensitive to ragweed pollen or house dust. First, it must be known whether the asthma is due to a sensitivity at all.

The basic mechanism of the allergic reaction is unknown. It is known that it appears to be an antigen-antibody reaction, that vasodilation and smooth muscle contraction account for the local symptoms, but it is not known why some persons produce such antibodies while others do not, why the reaction occurs in some tissues and not in others, why one becomes sensitive to a certain antigen and not to others, or why one may become sensitive to a substance to which he may have been exposed for many years. All these are unanswered questions because of lack of definite information as to the basic mechanism. At present there are many who are looking to the action of histamine to explain many of the problems, but even should that hypothesis prove correct the explanation for the antibody production is lacking.

Fundamentally, all allergic reactions are the same. There is edema, eosinophilic and lymphocytic infiltration and, when the reaction is often and frequently repeated, there may be necrosis or fibrosis or muscle hypertrophy resulting. Most allergic reactions are reversible, but irreversible changes may be found following recurring attacks. Wherever the reaction may occur the differences in cellular and tissue reactions and the symptoms are dependent upon the type of tissue involved and its location. The presenting symptom may be headache or intestinal colic, depending solely upon the location of the reaction.

Respiratory allergy is simply an allergic response in the respiratory tract. The reaction is the same as that elsewhere. There is no fundamental difference between hay fever and asthma. The differences are due solely to the tissues involved in the different locations.

For purposes of discussion, asthma may be divided into allergic and non-allergic; seasonal and perennial; extrinsic and intrinsic; infectious and non-infectious, and psychosomatic and organic.

These groups are not mutually exclusive, for asthma may be perennial and infectious; it may be non-allergic and psychosomatic and perennial. But it may be worth while to consider asthma from these different viewpoints to show the significance of them.

The terms allergy and allergic should be restricted to conditions due to an antigen-antibody mechanism, for it was this that was contemplated by von Pirquet when he proposed these terms. If asthma is purely psychosomatic in origin, it may be true asthma, but it is not an allergic condition. If intrinsic asthma is not related to sensitivity to any antigen, it may be true asthma, but it is not allergic. This may be considered quibbling, but such a distinction may help to clarify the thinking about these conditions.

If those limiting their work to this field, but working in different parts of the country, should be asked what part of the asthma they see is believed to be allergic, that is, on an immunologic basis, the answers would vary widely. It is a remarkable thing that competent physicians may reply that not more than 50 per cent of the asthma which they see is truly allergic—the other 50 per cent is due to other causes. Others, equally competent and equally honest, will state that probably 90 per cent of the asthma they see is allergic. The explanation of this disparity may be apparent upon further discussion of the classification.

There can be no argument, of course, as to whether asthma is seasonal or perennial. The history, if at all satisfactory, will offer this information. It is an important distinction to make, even though it is simple. Seasonal asthma, like seasonal hay fever, is almost without exception due to pollen. The asthma coincides with the blooming period of the plant to which the patient is sensitive and is absent the rest of the year. Treatment of these patients gives rather satisfactory results. For an unknown reason, pollen asthma responds better to pollen therapy than does hay fever. But the point of greatest importance is that seasonal asthma due to pollen seldom develops into perennial, chronic asthma. This is not an infallible rule, but pollen asthma rarely is a forerunner of chronic asthma.

Infectious asthma is a term applied to a wheezing dyspnea associated with symptoms of infection in the respiratory tract. In some parts of the country, the diagnosis of infectious asthma is made frequently. In fact, it may make up a large part of the total. On the other hand, some investigators believe that infectious asthma is an uncommon condition and the diagnosis seldom justified. How can we account for this difference?

The first allergic reaction which was recognized as such was the tuberculin reaction. Allergic reaction to bacteria is theoretically possible; there can be no objection to the diagnosis on this basis. But no one has yet been able to establish the fact that any asthma is due to an immunologic reaction to bacteria: Skin tests may show positive reaction to bacteria from the sputum or from other materials, but such a reaction may mean only that the patient has been sensitized to that organism, possibly months or years previously. It is not dependable evidence that the present asthma is due to the sensitivity. Again, as was learned in the days of toxin-antitoxin, children who had been injected with this mixture might subsequently show positive skin reactions to horse serum yet have no clinical sensitivity to it. Those who have worked most with test extracts of bacteria and with vaccines in treatment will usually be the first to admit the insecurity in depending upon them.

In many instances patients state that asthma started soon after the occurrence of some infection. Commonly patients report that attacks occur with colds, and, of course, sinusitis or bronchial infection may be concurrent with asthma. On this basis, many diagnoses of infectious asthma are made. These factors do not justify such a diagnosis. A mother may state that her child first had asthma following whooping cough, measles, mumps or other infection, and that the attacks are restricted largely or entirely to the times when he has a cold. In these cases it is as common to find some food or environmental factor responsible for the asthma as it is in the cases in which there is no association with any infection.

It should be remembered that there are factors which may precipitate attacks of asthma, but do so only in the patient who is allergic to some antigen. For example, a patient may be allergic to egg and yet have attacks of asthma only when he has a cold, when the weather changes suddenly, or with an emotional upset. In these instances, the cold is not the primary cause of the asthma, as may be shown by the fact that if the offending food is kept out of his diet, he may have a cold but not asthma with it. In other words, the food to which he is sensitive is the basic factor, but the sensitivity may be slight and he may be able to eat the food without asthma when he has no cold, the weather does not change or he has no emotional disturbance. But if he continues to eat the reacting food and then has a cold, the two together will produce an attack. As a friend remarked, "The antigen loads the gun and the cold pulls the trigger." There is abundant evidence that this explanation is correct.

If patients who are believed to be truly allergic are removed from the classification of "infectious" asthma, how many of those truly infectious are left? In some parts of the country the remainder may be considerably greater than in others. But it is difficult to form any acceptable statement until there is agreement at least on the interpretation of symptoms. That ought to be simple, but queerly enough, it is not.

There are those investigators who divide asthma into the extrinsic and intrinsic types, while others do not accept this as a valid division. Those who do, believe that in some people asthma develops without evidence of sensitivity to any external substance,

but due to some metabolic or other type of aberration within the body. The patients are said to be usually past middle life at the time of onset of the asthma, their attacks are not separate but continuous, nothing can be found to account for it, the condition is progressive and not controllable except as help may be had for brief periods by medication, and the death rate is high. Clinically, intrinsic asthma is said to differ definitely from that which may be called extrinsic, and the prognosis is much worse.

It is a very interesting fact that there are many investigators who are sure that in a considerable number of patients with asthma the disease may be classified as intrinsic in origin, while there are others probably of equal intelligence and with equal experience who say that such patients have not been observed by them. How can such divergence of opinion be explained? Since there is a great deal of difference in the mortality rates associated with the two types, it is a matter of importance to differentiate them accurately. Is the diagnosis of intrinsic asthma erroneous and do these patients have extrinsic asthma which has not been adequately diagnosed from an etiologic standpoint? There are those who think so. Or are those in the other camp failing to make a valid and important distinction? Or is it possible that both groups are right and that the difference may be due to geographic, climatic or other differences? The author has observed only one patient who met all of Rackemann's criteria for intrinsic asthma. In that patient it developed in middle life, it was continuously progressive and uncontrolled, and after seven years of futile effort to find relief, the patient died. If there is such a condition as intrinsic asthma, this was an example of it. The queer thing is that this is the only case of asthma observed by the author which was felt to belong in the "intrinsic" classification. Many cases of asthma for which there was no adequate explanation have been oserved, although it is believed that there was such an explanation and it merely was not found. And these unexplained cases were not, by accepted clinical standards, intrinsic asthma. If in 30 years of experience, only one case which seems to conform to the clinical picture of intrinsic asthma has been observed, it would seem that the condition is not common in the part of the world in which the author works.

As was stated previously, in some parts of the country asthma is considered infectious because it is associated with a certain clinical history. Similar historical correlations were noted in patients observed by the author, but they were not interpreted as indicating allergic disease due to infection. The difference here is in the interpretation of the patient's history and not in finding, or failing to find, a certain clinical syndrome. Physicians may differ as to how to interpret statements, but there should be no difficulty in seeing the same symptoms when competent observers are seeing them. And the author believes that many physicians do not see the syndrome labeled "intrinsic asthma." Therefore there must be cases of this kind much more frequently in some parts of the country than in others, and it is probably neither kind nor wise to insist that there is no such thing. But the fact remains that resolving this question is a matter of more than academic interest and deserves attention.

PSYCHOSOMATIC ASTHMA

Aside from the disagreement regarding the diagnosis of infectious asthma and as to the validity of the diagnosis of intrinsic asthma, it would seem that there ought to be some common ground on which agreement could be reached. But not yet. There still remains the matter of so-called psychosomatic asthma. And here again there is much argument and little agreement.

Everyone probably will admit that emotional states may play a part in the precipitation of allergic reactions. This is a familiar kind of response. Asthma attacks apparently induced by an emotional disturbance have been observed; urticarial attacks resulting from psychic upsets appear to be fairly common. Possibly allergic reactions of all kinds may be definitely influenced by the emotions.

But this is not the problem on which there is such definite—and sometimes so violent—disagreement. What is needed to know, and what some investigators affirm and others vigorously deny, is whether emotional disturbances in and of themselves can produce the allergic state or, to be technically accurate, reactions indistinguishable from the allergic reaction. For it may be said here, if there is such a thing as a psychosomatic asthma, it is not allergic. It may be asthma.

Some psychiatrists assert that asthma is frequently due entirely to resentments, frustrations, feelings of guilt, and other psychic states. They would exclude all other factors and make this the entire explanation for the somatic symptoms. Allergy would be relegated to a minor position as a cause of trouble. Opposed are many investigators who believe that emotional disturbances play only an accessory role and that the basic mechanism is that of allergy.

Where the truth lies cannot be said now. The author's belief is that it lies somewhere between these extremes; that allergic reactions may be precipitated or modified by emotional states, but that, with comparatively few exceptions, these are accessory and not the basic factor. Accurate information on which to base an unbiased belief will not be available until both those working in the field of psychiatry and those in the field of allergy are willing to cooperate in an unbiased fashion in the study of many patients.

Probably not so important, because it does not involve fundamental considerations of theory, is the question of the importance of allergy to foods. It is a good illustration of the need for straight thinking and objective clinical investigation. It would seem that after 30 years of clinical work in allergy, there

should be decision as to just how important foods are as the cause of asthma, but opinions are as widely separated as the poles. There are those who believe that foods are the most frequent and the most important etiologic factors and those who believe that foods may safely be disregarded as the cause of asthma. How can this variance be explained? There are probably two or three reasons involved. First, there may easily be a geographic or climatic variation. It may be that in some areas pollens are abundant, respiratory infections very common and industrial dusts considerable. It is quite possible, under such conditions, that the incidence of asthma due to sensitivity to food may be relatively less important. On the other hand, in an area where pollen is less, respiratory infections infrequent, and atmospheric contamination with industrial dusts and fumes largely absent, there may be few patients with asthma from these causes and the proportion of food-sensitive persons hence increased. Second, and possibly more important, is the fact that many allergists, while trying to be scientific in attitude, are in reality refusing to admit the error of an idea because the idea was originally accepted without critical thinking and was never afterward subjected to unbiased thinking and clinical trial. It seems incredible that intelligent men should still sneer at each other about belief in or against the role of food as an allergen. Surely it is susceptible of proof, and men who want to know the truth rather than to support their own beliefs should be able to determine just where the truth lies. The correct answer to this question is long overdue.

Every scientific physician realizes the difficulty of reaching safe conclusions in clinical practice. There is such a great number of variables involved in the treatment of human beings that one is justified in forming conclusions only after many and arduous observations over much time. Anything less than this leads to error, as some have had occasion to realize. For this reason, answers to our problems cannot be expected at once although they are badly needed. But the questions of the role of infection in asthma, the validity of a diagnosis of intrinsic asthma, and the extent of the influence of psychic states upon the production of asthma are of vital importance because both morbidity and mortality rates are influenced greatly by the answers.

These are some of the problems involved in the diagnosis of asthma. As has been stated, the differentiation of asthma from other conditions attended by dyspnea is usually not a very difficult task. But a consideration of the foregoing statements illustrates the difficulties attendant upon an etiologic diagnosis. These statements show that a correct diagnosis of the type of asthma is most important, for it determines the treatment and the outcome of the condition. And unfortunately, they show the complete lack of agreement as to such diagnoses. Also they show the opportunity for unbiased, careful observation. The days of clinical research are not gone.

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